SECTION ON MICROBIOLOGY

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Viruses and Neoplasms

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There is now conclusive evidence that viruses can cause cancer in a wide variety of species throughout the animal kingdom. Although there is no direct proof of the viral etiology of human cancer at present, there is little basis to refute the concept that viruses may be carcinogenic in man.

The exceedingly productive studies with animal tumor viruses have provided abundant knowledge about the relationship of viruses to cancer. It is now recognized that tumor viruses do not differ fundamentally from so-called classical viruses and that infection is not synonymous with disease. For example, many chickens and mice may carry latent leukemia viruses and never develop the disease. Much has been learned about the host factors which determine whether or not cancer will arise as a result of infection with a tumor virus.

A significant obstacle to human tumor virus research has been the lack of an optimal assay system. The carcinogenic potential of the animal tumor viruses in all instances was first demonstrated by injecting the suspected viruses into animals of the same species. This obviously poses serious difficulties with human studies, especially since injection in the newborn period was usually necessary and the latent periods for tumor appearance often approximated one-half of the animal's life span. The use of lower animals to assay human materials is often complicated by the presence of latent indigenous tumor viruses in the test animals. In one of our studies of human leukemic material, a virus which produces a high incidence of leukemia in mice was recovered after ten passages in mice. However, it has not been possible to demonstrate human origin of the agent and it probably represents a latent mouse leukemia virus which was somehow activated during the passages through mice.

Two human viruses, adenovirus 12 and 18, produce malignant tumors when injected into newborn hamsters. However, it is not known whether the same viruses are related to human cancer.

SV_{40} virus (monkey origin) also produces cancers in hamsters, and this virus was found in poliovirus and adenovirus vaccines which were given to large numbers of humans. It has not been established whether SV_{40} is carcinogenic for the human. However, a recent study of a group of children who were given poliovirus vaccine containing live SV_{40} virus when they were 6 to 8 years of age, indicated no increased cancer in this group during a four-year follow-up period. However, this does not prove that SV_{40} is innocuous in the human.

Electron microscopy of human leukemic tissue and plasma have shown particles which resemble the virus particles seen in mouse leukemia. However, the precise nature of these particles and their significance (if any) in the disease have not been established.

Recently, a strain of Rous sarcoma virus was shown to produce malignant tumors when inoculated into newborn monkeys. All seven monkeys in the experimental group developed tumors in two to six weeks.

A monkey virus (Yaba) which produces a benign tumor in the monkey was shown to produce the same kind of tumor in the human. The initial demonstration of human susceptibility resulted from a laboratory accident in which a laboratory assistant pricked his hand with a virus-contaminated needle.

Immunological Aspects of Virus Induction of Tumors

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With increasing evidence in recent years of the virus etiology of many types of tumors in animals and of immunological factors influencing tumor development in man and animals, it was to be expected that these two phenomena might be interrelated.

Indeed, it has been found that most, if not all, virus-induced tumors contain one or more new, "foreign" antigens which are not present in the normal cells of the host. Furthermore, these antigens appear to be specific, depending upon which virus caused their induction. In the case of polyoma-virus transformed cells in mice, the host's inability to recognize these foreign antigens and to reject them immunologically determines the appearance of a gross tumor. It has also been demonstrated that certain virus-induced tumors contain antigens to which the tumor-bearing host may react with specific complement-fixing antibodies.

To relate these findings from studies of virus-induced tumors of animals to the tumor problem of man may be helpful in determining the direction of the human investigations. If there exist viruses responsible for the induction of malignant transformation of human cells—and there is every reason to believe they do exist—then it seems likely that for their perpetuation in nature they would be widespread. As in the case of polyoma virus in mice, *infection* would be common in a large proportion of the population and not be limited to only those individuals who develop gross tumors as the result of that infection. Some other factor or factors would have to be responsible for determining which infected individual would later develop a clinically apparent tumor. The results of present investigations of virus tumors in animals suggest that one important factor determining this may be the ability of the individual to recognize and immunologically reject his own virus-transformed cells.

Current Concepts of Tumor Viruses

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At least three different types of virus-host cell interaction leading to neoplasia are now recognized. Neoplasia is a general and nonspecific type of cellular and tissue reaction, certain manifestations of which are common to the various separate disease entities that make up the over-all group of neoplastic diseases. Within this diversified group there are some specific viral neoplastic diseases, each of which is caused by the continuing action of a single virus or by members of closely related groups of viruses comparable to those responsible for specific diseases of other types. Other tumorigenic viruses act as biological carcinogens in much the same way as do nonviral carcinogenic agents, to bring about fundamental alterations in cells and endow them with neoplastic properties. The transformation is a heritable result of a rare chance interaction between viral and cellular genomes, rather than a continuing virus-cell interaction. Many common viruses that are not themselves tumorigenic are capable of enhancing the tumorigenic actions of carcinogenic chemicals.